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Supplementary Material 1. Influenza and non-influenza respiratory virus (NIRV) detection

Nasal/nasopharyngeal specimens were collected using Copan flocked swabs in Universal Transport Medium™ and refrigerated at 4°C until testing. All testing was at provincial public health reference laboratories in British Columbia (BCCDC Public Health Laboratory), Alberta (Alberta (Public Health Laboratory (ProvLab)), Ontario (Public Health Ontario Laboratory) and Quebec (Laboratoire de santé publique du Québec). All are accredited clinical and public health diagnostic and reference laboratories subject to regular proficiency testing programs, conducted at least thrice annually.

In all provinces except Quebec, specimens were screened for influenza A and B viruses using validated in-house reverse-transcriptase polymerase chain reaction (rRT-PCR) assays. Regardless of influenza positivity, specimens were additionally tested for a panel of influenza and NIRV targets using commercial multiplex RT-PCR assays as specified in **Table S1a**. In Quebec, screening for influenza was also by commercial multiplex RT-PCR assay. Influenza and non-influenza respiratory virus (NIRV) targets included in multiplex assays are specified in **Table S1b**.

Alberta did not perform NIRV testing in 2015-16 or 2016-17; Ontario did not in 2015-16. These provinces were excluded from influenza and NIRV analyses those seasons. Panels used in Ontario did not detect the HKU1 type of coronavirus any season; however, in other provinces, HKU1 comprised only a minority of coronaviruses detected overall (53/349; 15%). During the 2015-16 and 2016-17 seasons, the NIRV panel used in British Columbia and Quebec included three atypical bacteria targets; however, just five specimens included in the current study tested positive for one of these bacterial targets including three in British Columbia in 2016-17 and one each season from Quebec. For the current study, these bacterial targets were not taken into account.

Table S1a. Influenza and NIRV assays by season and province, 2010-11 to 2016-17

Season, Viral target	Province and assay			
	Alberta	British Columbia	Ontario	Quebec
2010-11				
Influenza	rRT-PCR	rRT-PCR[a]	rRT-PCR	QIAGEN ResPlex II v2
NIRV	Luminex® xTAG® RVP	Luminex® xTAG® RVP FAST	Seeplex® RV12 ACE	
2011-12				
Influenza	rRT-PCR	rRT-PCR[a]	rRT-PCR	Luminex® xTAG® RVP FAST
NIRV	Luminex® xTAG® RVP	Luminex® xTAG® RVP FAST	Seeplex® RV15 ACE	
2012-13				
Influenza	rRT-PCR	rRT-PCR[a]	rRT-PCR	Luminex® xTAG® RVP FAST
NIRV	Luminex® xTAG® RVP	Luminex® xTAG® RVP FAST	Seeplex® RV15 ACE	
2013-14				
Influenza	rRT-PCR	rRT-PCR[a]	rRT-PCR	Luminex® xTAG® RVP FAST v2
NIRV	Luminex® xTAG® RVP	Luminex® xTAG® RVP FAST	Seeplex® RV15 ACE	
2014-15				
Influenza	rRT-PCR	rRT-PCR[a]	rRT-PCR	Luminex® xTAG® RVP FAST v2
NIRV	Luminex® xTAG® RVP[b]	Luminex® xTAG® RVP FAST	Seeplex® RV15 ACE	
2015-16				
Influenza	rRT-PCR	rRT-PCR[a]	rRT-PCR	Luminex® xTAG® RVP FAST v2 and Luminex® NxTAG® RPP[c]
NIRV	—	Luminex® xTAG® RVP FAST and Luminex® NxTAG®[d]	—	
2016-17				
Influenza	rRT-PCR	rRT-PCR[a]	rRT-PCR	Luminex® NxTAG® RPP
NIRV	—	Luminex® NxTAG®	Allplex™ Respiratory	

NIRV = Non-influenza respiratory virus; rRT-PCR=reverse transcriptase real time polymerase chain reaction; "—" indicates NIRV testing not undertaken

[a] In BC, the influenza screening rRT-PCR assay included an additional target for respiratory syncytial virus (RSV).
[b] A subset of influenza-positive specimens from Alberta during the 2014-15 season were retrospectively tested for NIRVs in BC using the Luminex® NxTAG® Respiratory Pathogen Panel.
[c] In 2015-16, Quebec switched mid-season from the Luminex® xTAG® RVP FAST v2 to the Luminex® NxTAG® panel
[d] In 2015-16, BC switched mid-season from the Luminex® xTAG® RVP FAST to the Luminex® NxTAG® panel.

Table S1b. Influenza and NIRV targets on commercial multiplex RT-PCR assays by season and province, 2010-11 to 2016-17

Assay	QIAGEN	Seegene®			Luminex®					
	ResPlex II v2	Seeplex® RV12 ACE	Seeplex® RV15 ACE	Allplex™ Respiratory	xTAG® RVP	xTAG® RVP FAST		xTAG® RVP FAST v2	NxTAG® RPP[a]	
Province(s)	Quebec	Ontario			Alberta	British Columbia	Quebec	Quebec	British Columbia	Quebec
Season(s)	2010-11	2010-11	2010-11 to 2014-15	2016-17	2010-11 to 2014-15	2010-11 to 2015-16	2010-11 to 2013-14	2013-14 to 2015-16	2015-16 to 2016-17	
Adenovirus (combined)	--	✓	✓	✓	✓	✓		✓	✓	
Adenovirus B	✓	--	--	--	--	--		--	--	
Adenovirus E	✓	--	--	--	--	--		--	--	
Bocavirus	✓	--	✓	✓	--	✓		✓	✓	
Coronavirus 229E/NL63 (combined)	--	✓	✓	--	--	--		--	--	
Coronavirus 229E	✓	--	--	✓	✓	✓		✓	✓	
Coronavirus NL63	✓	--	--	✓	✓	✓		✓	✓	
Coronavirus OC43	✓	✓	✓	✓	✓	✓		✓	✓	
Coronavirus HKU1	✓	--	--	--	✓	✓		✓	✓	
Coxsackie/echovirus	✓	--	--	--	--	--		--	--	
Enterovirus/Rhinovirus (combined)	--	--	--	--	✓	✓		✓	✓	
Enterovirus	✓	--	✓	✓	--	--		--	--	
Rhinovirus	✓	✓	✓	✓	--	--		--	--	
HMPV	✓	✓	✓	✓	✓	✓		✓	✓	
Influenza A	✓	✓	✓	✓	✓	✓		✓	✓	
Influenza B	✓	✓	✓	✓	✓	✓		✓	✓	
Influenza A H1 subtype	--	--	--	✓	✓	✓		✓	✓	
Influenza A 2009 H1N1	--	--	--	✓	--	✓		✓	✓	
Influenza A H3 subtype	--	--	--	✓	✓	✓		✓	✓	
Parainfluenza 1	✓	✓	✓	✓	✓	✓		✓	✓	
Parainfluenza 2	✓	✓	✓	✓	✓	✓		✓	✓	
Parainfluenza 3	✓	✓	✓	✓	✓	✓		✓	✓	
Parainfluenza 4	✓	--	✓	✓	✓	✓		✓	✓	
RSV (combined)	--	--	--	--	--	✓		✓	--	
RSV type A	✓	✓	✓	✓	✓	--		--	✓	
RSV type B	✓	✓	✓	✓	✓	--		--	✓	

NIRV= non-influenza respiratory virus; HMPV=human metapneumovirus; RPP=respiratory pathogen panel; RSV=respiratory syncytial virus; RVP=respiratory virus panel

[a] Atypical bacterial targets additionally include *Chlamydophila pneumoniae, Legionella pneumophila and Mycoplasma pneumoniae*.

Supplementary Material 2. Sensitivity analyses: odds ratios for influenza vaccine effect against influenza and NIRV, Canadian SPSN, 2010-11 to 2016-17

Odds ratios (OR) for influenza vaccine effect against influenza and non-influenza respiratory viruses (NIRV), individually and in combination, were derived by test-negative design using historic datasets of the Canadian Sentinel Practitioner Surveillance Network (SPSN) spanning the 2010-11 to 2016-17 seasons. Estimates derived as in the main manuscript are compared to sensitivity modifications.

In **Table S2a**, sensitivity analysis includes comparison of ORs that were unadjusted, adjusted for age alone, adjusted for age group and other covariates included in primary analysis (province, specimen collection interval, calendar time and season), and also additionally adjusting for comorbidity and sex. For all models, participants missing complete covariate information were excluded. Comorbidity information was missing for about 6% of influenza, coronavirus, NIRV combined cases and respective controls; sex information was missing for <1%. For models adjusting for comorbidity and sex, participants missing information for these additional covariates were also excluded compared to primary analysis.

In **Table S2b**, sensitivity analyses compare unadjusted and adjusted ORs excluding or including cases of co-infection across NIRV groupings. Note that influenza co-infections were still excluded from all NIRV analyses.

Table S2a. Sensitivity analysis: adjusting for age and other covariates, without (primary) or with comorbidity and sex

Target pathogen[a]	Primary analysis: without comorbidity and sex as covariates (excludes participants missing covariate information: age, province, specimen collection interval, calendar time, season)					Sensitivity analysis: with comorbidity and sex as covariates (excludes participants missing covariate information: age, province, specimen collection interval, calendar time, season, plus comorbidity, sex)				
	Test-positive Cases[b]	Test-negative Controls[c]	Unadjusted OR (95%CI)	Adjusted for age only[d] OR (95%CI)	Adjusted as per primary[e] OR (95%CI)	Test-positive Cases[b]	Test-negative Controls[c]	Unadjusted OR (95%CI)	Adjusted as per primary[e] OR (95%CI)	Adjusted as per primary plus comorbidity and sex[f] OR (95%CI)
Influenza										
Vaccinated	843	1963	0.58 (0.53, 0.63)	0.57 (0.51, 0.62)	0.55 (0.50, 0.61)	800	1858	0.57 (0.52, 0.63)	0.55 (0.50, 0.61)	0.56 (0.51, 0.63)
Unvaccinated	3438	4618	Reference	Reference	Reference	3209	4275	Reference	Reference	Reference
Non-influenza respiratory viruses (NIRV) combined										
Vaccinated	817	1101	1.16 (1.04, 1.30)	1.16 (1.03, 1.30)	1.11 (0.99, 1.26)	776	1040	1.16 (1.04, 1.30)	1.11 (0.98, 1.26)	1.10 (0.97, 1.25)
Unvaccinated	1748	2740	Reference	Reference	Reference	1627	2537	Reference	Reference	Reference
Coronavirus (CoV)										
Vaccinated	187	1756	1.17 (0.97, 1.40)	1.10 (0.91, 1.34)	1.04 (0.85, 1.28)	181	1657	1.19 (0.99, 1.44)	1.07 (0.87, 1.32)	1.05 (0.85, 1.30)
Unvaccinated	383	4191	Reference	Reference	Reference	356	3885	Reference	Reference	Reference
Entero-/Rhinovirus (EV/RV)										
Vaccinated	179	1758	0.89 (0.74,1.07)	0.93 (0.77, 1.13)	0.99 (0.82, 1.21)	169	1665	0.87 (0.73, 1.05)	0.99 (0.81, 1.22)	1.00 (0.81, 1.23)
Unvaccinated	466	4084	Reference	Reference	Reference	438	3775	Reference	Reference	Reference
Human metapneumovirus (HMPV)										
Vaccinated	146	1808	1.44 (1.16, 1.78)	1.34 (1.06, 1.68)	1.19 (0.95, 1.51)	138	1711	1.42 (1.14, 1.76)	1.18 (0.93, 1.51)	1.18 (0.92, 1.50)
Unvaccinated	244	4349	Reference	Reference	Reference	229	4024	Reference	Reference	Reference
Parainfluenza virus (PIV)										
Vaccinated	92	1862	0.96 (0.75, 1.24)	0.93 (0.71, 1.21)	0.96 (0.73, 1.26)	89	1760	0.99 (0.77, 1.27)	0.97 (0.73, 1.28)	0.99 (0.75, 1.32)
Unvaccinated	224	4366	Reference	Reference	Reference	207	4043	Reference	Reference	Reference
Respiratory Syncytial virus (RSV)										
Vaccinated	184	1759	1.30 (1.08, 1.57)	1.22 (0.99-1.50)	1.11 (0.89, 1.37)	171	1670	1.30 (1.07, 1.58)	1.07 (0.86, 1.34)	1.03 (0.82, 1.29)
Unvaccinated	340	4219	Reference	Reference	Reference	308	3919	Reference	Reference	Reference

NIRV = non-influenza respiratory virus; OR = odds ratio; CI = confidence interval

[a] Specimens that test positive for influenza virus were excluded from all analyses for which NIRVs were the target pathogen. Vaccinated participants who received vaccine <2 weeks prior to onset of influenza-like illness were excluded.

[b] Single detections, excluding co-infections across NIRV groupings

[c] Test-negative for the target pathogen; co-infections allowed among controls (except for influenza) but note that for NIRV combined analysis, control group is pan-negative

[d] Adjusted for age group (1-8, 9-19, 20-49, 50-64, ≥65 years).

[e] Adjusted for age group (as per footnote d) plus province (Alberta, British Columbia, Ontario, Quebec), specimen collection interval (≤4, 5-7 days), calendar time (based on week of specimen collection modelled as natural cubic spline functions with 3 equally spaced knots), and season (2010-11, 2011-12, 2012-13, 2013-14, 2014-15, 2015-16, 2016-17).

[f] Adjusted as per footnotes d and e and additionally for sex (male or female) and comorbidity (yes or no). Comorbidity defined as chronic medical conditions that place individuals at higher risk of serious complications from influenza as defined by Canada's National Advisory Committee on Immunization (NACI) including: heart, pulmonary (including asthma), renal, metabolic (such as diabetes), blood, cancer, or immune comprising conditions; conditions that compromise management of respiratory secretions and increase risk of aspiration; or morbid obesity (body mass index ≥40).

Table S2b. Sensitivity analysis: cases excluding (primary) or including co-infections

Target pathogen[a]	Primary analysis: excluding co-infections among cases				Sensitivity analysis: including co-infections among cases			
	Test-positive Cases[b]	Test-negative Controls[c]	Unadjusted OR (95%CI)	Adjusted[d] OR (95%CI)	Test-positive Cases[e]	Test-negative Controls[c]	Unadjusted OR (95%CI)	Adjusted[d] OR (95%CI)
Influenza								
Vaccinated	843	1963	0.58 (0.53, 0.63)	0.55 (0.50, 0.61)	899	1963	0.58 (0.53, 0.64)	0.56 (0.51, 0.62)
Unvaccinated	3438	4618	Reference	Reference	3633	4618	Reference	Reference
Non-influenza respiratory viruses (NIRV) combined								
Vaccinated	817	1101	1.16 (1.04, 1.30)	1.11 (0.99, 1.26)	862	1101	1.14 (1.03, 1.27)	1.12 (0.99, 1.26)
Unvaccinated	1748	2740	Reference	Reference	1878	2740	Reference	Reference
Coronavirus (CoV)								
Vaccinated	187	1756	1.17 (0.97, 1.40)	1.04 (0.85, 1.28)	207	1756	1.16 (0.97, 1.38)	1.08 (0.89, 1.31)
Unvaccinated	383	4191	Reference	Reference	427	4191	Reference	Reference
Entero-/Rhinovirus (EV/RV)								
Vaccinated	179	1758	0.89 (0.74,1.07)	0.99 (0.82, 1.21)	205	1758	0.89 (0.75, 1.06)	1.03 (0.85, 1.24)
Unvaccinated	466	4084	Reference	Reference	534	4084	Reference	Reference
Human metapneumovirus (HMPV)								
Vaccinated	146	1808	1.44 (1.16, 1.78)	1.19 (0.95, 1.51)	155	1808	1.39 (1.13, 1.70)	1.20 (0.95, 1.50)
Unvaccinated	244	4349	Reference	Reference	269	4349	Reference	Reference
Parainfluenza virus (PIV)								
Vaccinated	92	1862	0.96 (0.75, 1.24)	0.96 (0.73, 1.26)	101	1862	0.94 (0.74, 1.19)	0.98 (0.76, 1.27)
Unvaccinated	224	4366	Reference	Reference	252	4366	Reference	Reference
Respiratory Syncytial virus (RSV)								
Vaccinated	184	1759	1.30 (1.08, 1.57)	1.11 (0.89, 1.37)	204	1759	1.23 (1.03, 1.46)	1.10 (0.90, 1.35)
Unvaccinated	340	4219	Reference	Reference	399	4219	Reference	Reference

NIRV = non-influenza respiratory virus; OR = odds ratio; CI = confidence interval

[a] Specimens that test positive for influenza virus were excluded from all analyses for which NIRVs were the target pathogen. Vaccinated participants who received vaccine <2 weeks prior to onset of influenza-like illness were excluded.

[b] Single detections, excluding co-infections across NIRV groupings from cases (co-infections within NIRV groupings retained, e.g. multiple coronavirus infections)

[c] Test-negative for the target pathogen; co-infections allowed among controls (except for influenza) but note that for NIRV combined analysis, control group is pan-negative

[d] Adjusted for age group (1-8, 9-19, 20-49, 50-64, ≥65 years), province (Alberta, British Columbia, Ontario, Quebec), specimen collection interval (≤4, 5-7 days), calendar time (based on week of specimen collection modelled as natural cubic spline functions with 3 equally spaced knots), and season (2010-11, 2011-12, 2012-13, 2013-14, 2014-15, 2015-16, 2016-17).

[e] Cases include co-infections across NIRV groupings but influenza test-positive specimens still excluded from cases and controls for NIRV analyses

Supplementary Material 3. Core prerequisite for TND analysis of influenza vaccine effects on NIRV: impact of including or excluding influenza cases from the control group

In analysis of vaccine effectiveness (VE) by test-negative design (TND), the likelihood of vaccination is compared between test-positive cases and test-negative controls through the odds ratio (OR), adjusted for potential confounders and with VE derived as $(1–OR_{adjusted}) \times 100\%$. Valid VE estimation by TND requires vaccine to have no effect on alternate etiologies of the same clinical syndrome, included in the control group [1]. As a core prerequisite of TND analysis, therefore, etiologies against which vaccine is effective should be excluded from the test-negative control group, and this applies also when exploring vaccine effects against non-vaccine target pathogens.

This core prerequisite for valid VE estimation by TND is illustrated for influenza vaccine effects against non-influenza respiratory viruses (NIRV) in **Table S3** below in which we have re-analyzed data adapted from the study by Wolff (univariate analyses available only) [2] as well as the Canadian Sentinel Practitioner Surveillance Network (SPSN) (univariate and adjusted). In this re-analysis of both data sets, we compare ORs *properly* excluding influenza test-positive specimens from the control group (in compliance with the TND core requirement) and *improperly* including influenza test-positive specimens within the control group (in violation of the TND core requirement, presented for illustrative purposes only).

In the context of effective influenza vaccine, cases of influenza would have lower likelihood of vaccination; as such, their inclusion would tend to reduce the proportion vaccinated in the control group and inflate ORs in TND comparison of vaccine exposure between cases and controls. Indeed, as shown in both data sets and for all NIRV outcomes explored, ORs for influenza vaccination become biased higher with *improper* inclusion of influenza test-positive specimens amongst controls. In both data sets this reflects the systematically reduced likelihood of vaccination (i.e. proportion vaccinated) when influenza cases are included within the control group.

References:

1. De Serres G, Skowronski DM, Wu XW, Ambrose CS. The test-negative design: validity, accuracy and precision of vaccine efficacy estimates compared to the gold standard of randomised placebo-controlled clinical trials. Euro Surveill 2013; Sept 12;18(37). Pii:20585. DOI: 10.2807/1560-7917.es2013.18.37.20585

2. Wolff GG. Influenza vaccination and respiratory virus interference among Department of Defense personnel during the 2017–2018 influenza season. Vaccine. 2020 Jan 10;38(2):350-4

Table S3. Odds ratio (OR) for influenza vaccination among NIRV cases versus test-negative control groups that do or do not include influenza virus positive specimens, adapted from Wolff and the Canadian Sentinel Practitioner Surveillance Network (SPSN)

Target pathogen	Influenza Vaccination	Data from Wolff, 2017-18 season [2]				Data from Canadian SPSN, 2010-11 to 2016-17 seasons			
		Cases[a]	Controls[b]	Unadjusted OR (95%CI)	p value	Cases	Controls[a]	Unadjusted OR (95%CI)	Adjusted[c] OR (95%CI)
Non-influenza respiratory virus (NIRV)									
Cases: NIRV positive specimens Controls: NIRV pan-negative specimens, ***properly excluding influenza positive***	Vaccinated	2050	2441	0.81[d] (0.72, 0.91)	<0.01	817	1101	1.16 (1.04, 1.30)	1.11 (0.99, 1.26)
	Unvaccinated	830	799			1748	2740		
	% Vaccinated	71%	75%			32%	29%		
Cases: NIRV positive specimens Controls: NIRV pan-negative specimens, ***improperly including influenza positive***	Vaccinated	2050	4491	1.15 (1.05, 1.27)	<0.01	817	1944	1.49 (1.35, 1.64)	1.47 (1.32, 1.63)
	Unvaccinated	830	2098			1748	6178		
	% Vaccinated	71%	68%			32%	24%		
Coronavirus (CoV)									
Cases: CoV positive specimens Controls: CoV negative specimens and ***properly excluding influenza positive***	Vaccinated	507	3984	1.09 (0.91, 1.31)	0.35	187	1756	1.17 (0.97, 1.40)	1.04 (0.85, 1.28)
	Unvaccinated	170	1459			383	4191		
	% Vaccinated	75%	73%			33%	30%		
Cases: CoV positive specimens Controls: CoV negative specimens, but ***improperly including influenza positive***	Vaccinated	507	6034	1.36 (1.14, 1.63)	<0.01	187	2635	1.44 (1.2, 1.72)	1.33 (1.09, 1.62)
	Unvaccinated	170	2758			383	7758		
	% Vaccinated	75%	69%			33%	25%		
Enterovirus/Rhinovirus (EV/RV)									
Cases: EV/RV positive specimens Controls: EV/RV negative specimens and ***properly excluding influenza positive***	Vaccinated	875	3616	0.74 (0.65, 0.85)	<0.01	179	1758	0.89 (0.74,1.07)	0.99 (0.82, 1.21)
	Unvaccinated	400	1229			466	4084		
	% Vaccinated	69%	75%			28%	30%		
Cases: EV/RV positive specimens Controls: EV/RV negative specimens, but ***improperly including influenza positive***	Vaccinated	875	5666	0.98 (0.86, 1.11)	0.71	179	2642	1.11 (0.93, 1.33)	1.22 (1.01, 1.49)
	Unvaccinated	400	2528			466	7643		
	% Vaccinated	69%	69%			28%	26%		
Human metapneumovirus (HMPV)									
Cases: HMPV positive specimens Controls: HMPV negative specimens and ***properly excluding influenza positive***	Vaccinated	335	4156	1.22 (0.97, 1.53)	0.09	146	1808	1.44 (1.16, 1.78)	1.19 (0.95, 1.51)
	Unvaccinated	101	1528			244	4349		
	% Vaccinated	77%	73%			37%	29%		
Cases: HMPV positive specimens Controls: HMPV negative specimens, but ***improperly including influenza positive***	Vaccinated	335	6206	1.51 (1.20, 1.90)	<0.01	146	2702	1.76 (1.43, 2.18)	1.57 (1.25, 1.97)
	Unvaccinated	101	2827			244	7970		
	% Vaccinated	77%	68%			37%	25%		
Parainfluenza virus (PIV)									
Cases: PIV positive specimens Controls: PIV negative specimens and ***properly excluding influenza positive***	Vaccinated	139	4352	0.53 (0.41, 0.70)	<0.01	92	1862	0.96 (0.75, 1.24)	0.96 (0.73, 1.26)
	Unvaccinated	92	1537			224	4366		
	% Vaccinated	60%	74%			29%	30%		
Cases: PIV positive specimens Controls: PIV negative specimens, but ***improperly including influenza positive***	Vaccinated	139	6402	0.67 (0.51, 0.87)	<0.01	92	2754	1.19 (0.93, 1.52)	1.17 (0.89, 1.53)
	Unvaccinated	92	2836			224	7989		
	% Vaccinated	60%	69%			29%	26%		

[a] Test-positive cases without co-infections across NIRV-groupings.

[b] Test-negative controls still allow for co-infections involving other viruses whereas cases exclude all co-infections. Note that this does not apply to NIRV combined for which controls are all NIRV-negative.

[c] All analyses adjusted for age group (1-8, 9-19, 20-49, 50-64, ≥65 years), province (Alberta, British Columbia, Ontario, Quebec), specimen collection interval (≤4, 5-7 days), calendar time (based on week of specimen collection modelled as natural cubic spline functions with 3 equally spaced knots), and season (2010-11, 2011-12, 2012-13, 2013-14, 2014-15, 2015-16, 2016-17)..

[d] For NIRV, excluding influenza positive specimens, Wolff presents the age-adjusted OR as 0.97 (95% confidence interval (CI): 0.86, 1.09). For other combined or individual NIRV analyses, Wolff did not present adjusted estimates.

Target pathogen	Influenza Vaccination	Data from Wolff, 2017-18 season [2]				Data from Canadian SPSN, 2010-11 to 2016-17 seasons			
		Cases[a]	Controls[b]	Unadjusted OR (95%CI)	p value	Cases	Controls[a]	Unadjusted OR (95%CI)	Adjusted[c] OR (95%CI)
Respiratory Syncytial Virus (RSV)									
Cases: RSV positive specimens Controls: RSV negative specimens and ***properly excluding influenza positive***	Vaccinated	369	4122	0.63 (0.53, 0.76)	<0.01	184	1759	1.30 (1.08, 1.57)	1.11 (0.89, 1.37)
	Unvaccinated	202	1427			340	4219		
	% Vaccinated	65%	74%			35%	29%		
Cases: RSV positive specimens Controls: RSV negative specimens, but ***improperly including influenza positive***	Vaccinated	369	6172	0.81 (0.68, 0.96)	0.02	184	2652	1.60 (1.33, 1.92)	1.40 (1.13, 1.72)
	Unvaccinated	202	2726			340	7832		
	% Vaccinated	65%	69%			35%	25%		